N-terminal Pro-brain Natriuretic Peptide in Apparently Healthy Smokers.

Seenaa Badr Mohammed[1], Zainab Falah Hassan[2], Thanaa Mohammed Juda[3], Maan Abdulameer Kitab[4] , Zinah abbass ali[5]

1, 3, 5 College of Medicine-Babylon University, Iraq
2 College of Medicine-Babylon University, Iraq
4 Al-Hilla teaching hospital

Abstract

Background and objective

Smoking is a major cause of cardiovascular diseases. N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a valid negative biomarker of left ventricular (Lv) dysfunction. The current study investigated whether smoking has an effect on NT-proBNP serum level.

Methods:

A total of 44subjects 22smokers and 22 non smokers as controls were enrolled in the study. History of cardiovascular or pulmonary disease was an exclusion criterion. Serum levels of NT-proBNP were measured using an enzyme linked immunosorbent assay.

Results:

Analysis of data showed that there was a significant difference ($P < 0.05$, in serum NT-proBNP between smokers and controls.proBNP were 410 and 111 pg/ml in smokers and controls, respectively. Also, serum NT-proBNP level correlated with both average number of daily cigarettes smoked and body mass index of smokers.

Conclusion

These results showed that smoking could increase serum levels of NT-proBNP. Accordingly, an elevated NT-proBNP could be a strong predictor of Left ventricular dysfunction in smokers.

Keywords: N-terminal pro-brain natriuretic peptide, smoking, BMI, numbers of cigarettes

Introduction

Smoking is one of the leading causes of preventable death globally.[1] Male and female smokers lose an average of 13.2 and 14.5 years of life, respectively.[2] At least half of all lifelong smokers die earlier as a result of smoking. [3] According to the WHO, tobacco kills around six million individuals a year worldwide, including more than 600 000 nonsmokers who die from exposure to second-hand smoke. Since 1964, 2.5 million Americans have died from cardiovascular and pulmonary disease because of passive smoking.[1]

Smoking generally has adverse health effects, because smoke inhalation inherently poses challenges to various physiologic processes such as respiration .[4]Despite the ongoing worldwide smoking pan campaigns, complications of smoking remain a major health problems worldwide .

(NT-proBNP) peptide (also known as ventricular natriuretic peptide) is a 32-amino acid polypeptide secreted by the ventricles of the heart in response to excessive stretching of heart muscle cells. It had well-characterized diagnostic and prognostic indicators in several cardiovascular disorders. {5,6}

Atrial natriuretic peptide (ANP) and B-type natriuretic peptide (BNP) have important physiological roles in fluid homeostasis, vascular tone, and cardiac pathology, including myocardial ischemia and left ventricular dysfunction and remodeling. Studies have also assessed a possible connection

between natriuretic peptide concentrations and the risk of mortality in random populations, suggesting an association between plasma concentrations and mortality, independently of other risk factors.[7,8]

This study aims to reveal the effect of smoking on heart through serum level of NT-proBNP which is very stable [9,10] and is characterized by a longer half-life and higher concentrations than the mature hormone BNP [11] so we chose this markers in this study.

Materials and Methods

This case –control study was conducted in the laboratory of Biochemistry Department, College of Medicine , University of Babylon. 44 subjects enrolled in this study. Twenty two are apparently healthy smokers, other twenty two apparently healthy nonsmokers as a control group .All subjects have no history of chronic disease (as diabetes mellitus, hypertension inflammatory disease such as rheumatoid arthritis). Full history was taken from all subjects including: age, residence, medical history, drug history and surgical history.

Venous blood sample was collected and serum was isolated within 2 hours of collection from the subjects and immediately stored at −80°C. Serum brain natriuretic peptide was determined by using enzyme linked immunosorbent assay (ELISA) [12].

The statistical analysis was performed by using SPSS version 18 for windows. Data were expressed as Mean ± SE. Serum levels of NT-proBNP were compared between smokers and controls using an independent t-test. Pearson correlation analysis that have been used to determine the significant difference between the two groups. P values less than 0.05 is considered significant.

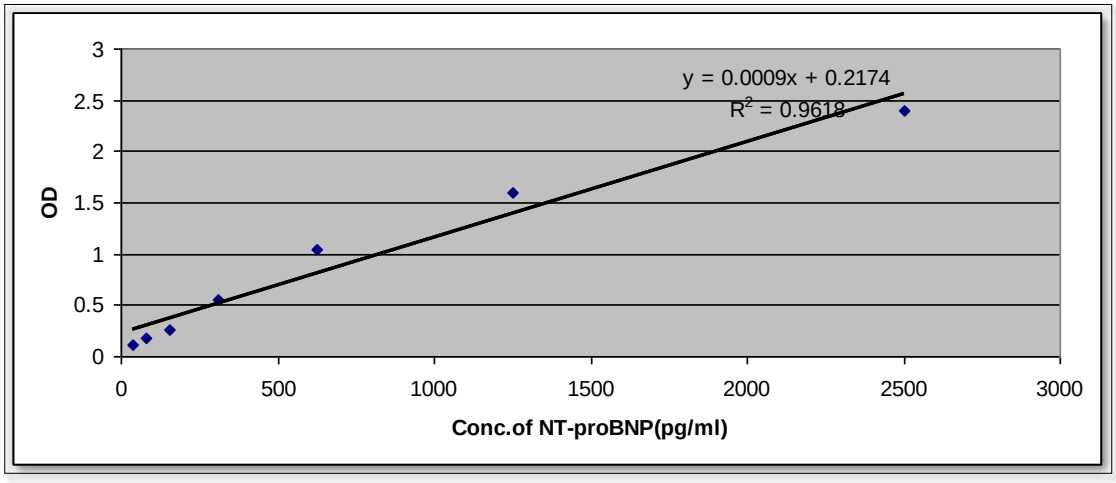

Figure 1. Standared curve of NT-proBNP

Results

Analysis of data showed that serum level of NT-proBNP in smoker with mean age of 34years and BMI mean of 27was significantly higher than its level in non-smokers as table (1) reveals

Table (1): Serum NT-proBNP levels in all subjects

Groups		Mean	Std. Error Mean	P value
NT	**smokers**	410	85	*0.01*
	Non-smokers	111	82	

Also the study revealed that there are positive correlation between serum level of NT-proBNP and average number of daily cigarettes smoked,age and BMI in smokers subjects but non-significant as figures (2,3and4) show.

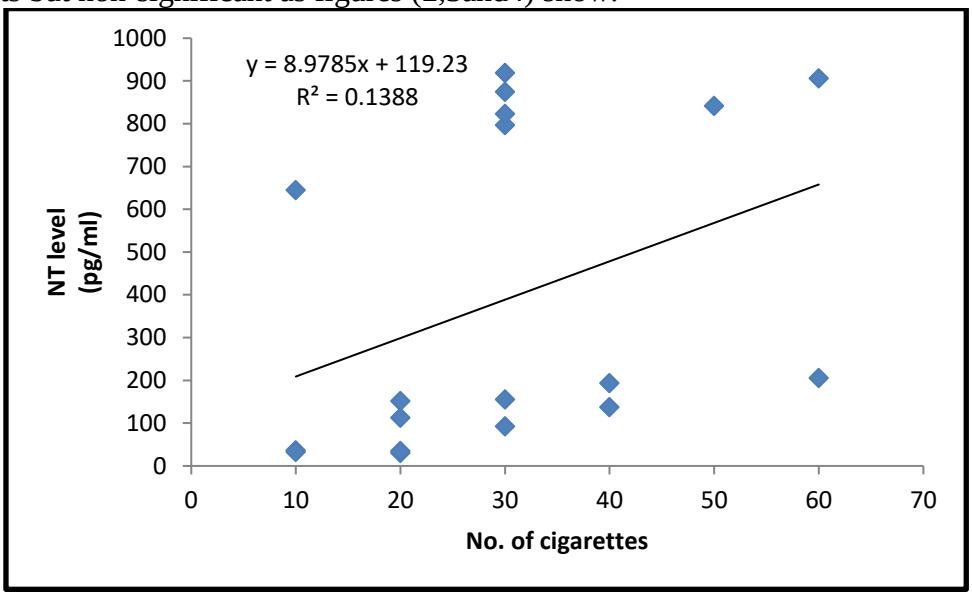

Figure 2. Correlation between level of NT-proBNP and average number of cigarettes smoked daily

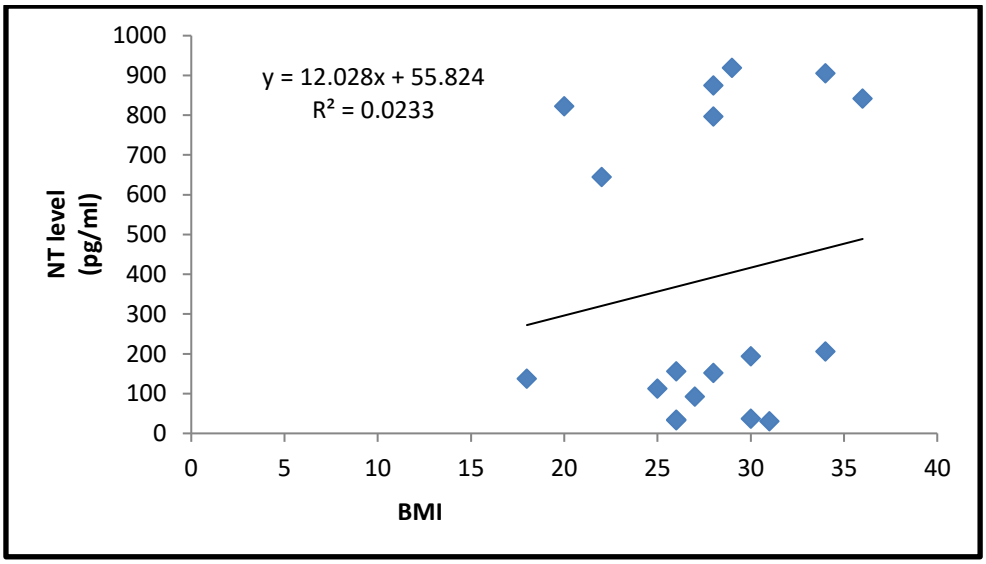

Figure 3. Correlation between level of NT-proBNP and BMI of smokers

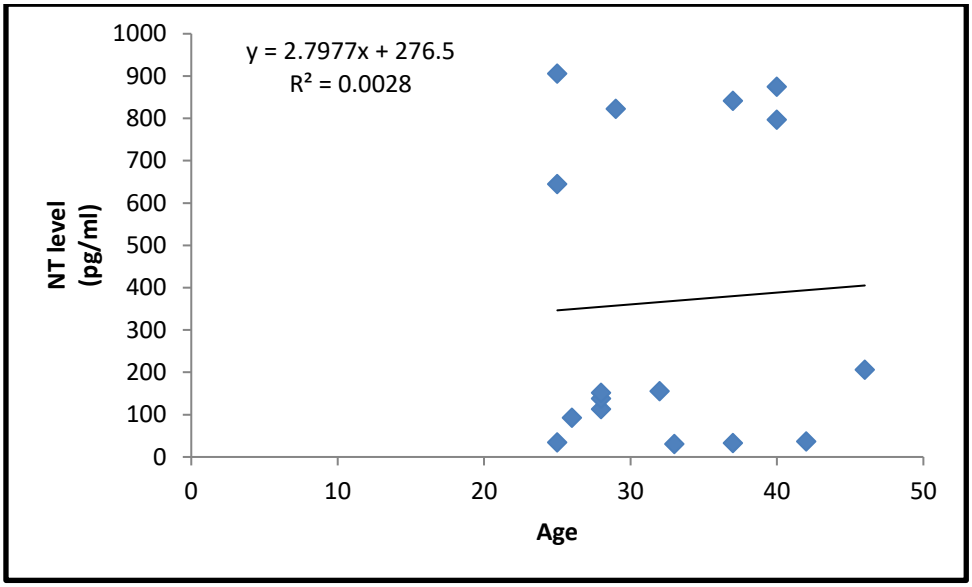

Figure 4. Correlation between level of NT-proBNP and age of smokers

Discussion

Ventricular stretch causes synthesis and production of BNP and NT-pro BNP which considered the biological active form [13-15] However, BNP levels are influenced by other factors such as age, gender, diabetes, and impaired renal function.[16]

In this study level of NT-pro BNP in smokers increased in compare to non smokers which may indicate that smoking cause stretching in cardiac wall and this is the underlying basis of cardiovascular diseases that associated with smoking, Our baseline findings are consistent with other reports showing that cigarette smoking increases cardiac overload.[17-19]

Also, the current study investigated the association between serum NT-proBNP and other variables that could have an effect on Lv function such age, and body weight. The results obtained showed an insignificant effect of age on serum NT-proBNP. These results are inconsistent with other researchers who found that NT-proBNP is higher in women and in older age groups[20,21] and also inconsistent with Lakatta *et al.* [22], who concluded that the use of age-dependent limits of NT-proBNP will increase the diagnostic accuracy and reduce missed diagnosis of Lv dysfunction, and rationalize echocardiographic follow-up. In addition, positive association of BNP level with the body mass index (BMI) has been reported in this study and this inconsistence with cross-sectional studies.[23–25]

Conclusion

We have shown that serum NT-proBNP is significantly higher in smokers than non smokers without overt cardiovascular or pulmonary disease. Accordingly, we recommended the use of serum NT-proBNP measurements to select smokers who are in need of further cardiovascular assessment tools such as echocardiography. However, there is still a need for further studies to investigate the relationship between various echocardiographic parameters and serum levels of NT-pro BNP.

References

1.Centers for Disease Control and Prevention (CDC) (2002). "Annual smoking-attributable mortality, years of potential life lost, and economic costs--United States, 1995-1999".MMWR Morb. Mortal. Wkly. Rep. 51 (14): 300–3.

2. Doll R, Peto R, Boreham J, Sutherland I and Peto Boreham; Sutherland (2004). "Mortality in relation to smoking: 50 years' observations on male British doctors". *BMJ;* 328 (7455):1519.

3.Thun MJ, Day-Lally CA, Calle EE, Flanders WD, Heath CW, Day-Lally, Calle; Flanders and Heath Jr (1995). "Excess mortality among cigarette smokers: changes in a 20-year interval". *Am J Public Health*; 85 (9): 1223–30.

4. West R and Shiffman S. (2007). Fast Facts: Smoking Cessation. *Health Press Ltd*; p. 28

5. Mueller T, Gegenhuber A, Dieplinger B, Poelz W and Haltmayer M. (2004). Long-term stability of endogenous B-type natriuretic peptide (BNP) and amino terminal proBNP (NT-proBNP) in frozen plasma samples. *Clin Chem Lab Med*; 42:942 – 4.

6. Pemberton CJ, Johnson ML, Yandle TG and Espiner EA. (2000). Deconvolution analysis of cardiac natriuretic peptides during acute volume overload. *Hypertension*; 36:355 -9.

7. Rubattu B, Calvieri C, Pagliaro B and Volpe M. (2013).Atrial natriuretic peptide and regulation of vascular function in hypertension and heart failure: implications for novel therapeutic strategies. *J.Hypertens*;6:1061-72.

8. Lauridsen B, Iversen K and Hunter I, et al.(2013).ProANP plasma measurement predicts all-cause mortality in acutely hospitalised patients: a cohort study. *BMJ Open*;3:e003288.

9. Barnes SC, Collinson PO, Galasko G, Lahiri A and Senior R.(2004). Evaluation of N-terminal pro-B type natriuretic peptide analysis on the elecsys 1010 and 2010 analysers. *Ann Clin Biochem*;41:459 – 63.

10. Mueller T, Gegenhuber A, Dieplinger B, Poelz Wand Haltmayer M.(2004). Long-term stability of endogenous B-type natriuretic peptide (BNP) and amino terminal proBNP (NT-proBNP) in frozen plasma samples. *Clin Chem Lab Med*;42:942 – 4.

11. Pemberton CJ, Johnson ML, Yandle TG and Espiner EA.(2000). Deconvolution analysis of cardiac natriuretic peptides during acute volume overload. *Hypertension*;36:355 – 9.

12. Human NT-proBNP (N-terminal pro-brain natriuretic peptide) ELISA Kit.Elabscience biotechnology Co.,Ltd

13. Kroll MH and Srisawasdi P. (2007). The clearance of BNP modeled using the NT-proBNP-BNP relationship. *Biosystems*;88:147-55.

14. Yeo K-TJ, Wu AHB and Apple FS, .(2003). Multicenter evaluation of the Roche NT-proBNP assay and comparison to the Bio site Triage BNP assay. *Clin Chim Acta*; 338:107-15.

15. Rawlins ML, Own WE and Roberts WL.(2005). Performance characteristics of four automated natriuretic peptide assays.*Am J Clin Pathol*.;123:439-45.

16. Lemos JAD.(2008). Biomarkers in Heart Disease. Antman E, ed. Malden, *MA: Blackwell Publishing*; 238.

17. Otsuka T1, Kawada T, Seino Y, Ibuki C, Katsumata M and Kodani E.(2010). Relation of smoking status to serum levels of N-terminal pro-brain natriuretic peptide in middle-aged men without overt cardiovascular disease. *Am J Cardiol*. ;106(10):1456-60

18.Wang TJ, Larson MG, Levy D, Benjamin EJ and Leip EP, et al. (2004) Plasma natriuretic peptide levels and the risk of cardiovascular events and death. *N Engl J Med* 350: 655–63.

19. Kistorp C, Raymond I, Pedersen F, Gustafsson F and Faber J, et al. (2005). N-terminal pro-brain natriuretic peptide, C-reactive protein, and urinary albumin levels as predictors of mortality and cardiovascular events in older adults. *JAMA*; 293: 1609–16.

20. Raymond I, Groenning BA, Hildebrandt PR, Nilsson JC, Bauman M and Trawinski J, et al.(2003). The influence of age, sex and other variables on the plasma level of N-terminal pro brain natriuretic peptide in a large sample of the general population. *Heart* ;89 :745-751

21. Hildebrandt P, Collinson PO, Doughty RN, Fuat A, Gaze DC and Gustafsson F, et al. (2010). Age-dependent values of N-terminal pro-B-type natriuretic peptide are superior to a single cutpoint for ruling out suspected systolic dysfunction in primary care. *Eur Heart J* ;31 :1881-9.

22. Lakatta EG and Levy D.(2003). Arterial and cardiac aging: major shareholders in cardiovascular disease enterprises: part I: aging arteries: a ′set up′ for vascular disease. *Circulation*; 107 :139-146.

23. Taylor JA, Christenson RH, Rao K, Jorge M and Gottlieb SS.(2006). B-type natriuretic peptide and N-terminal pro B-type natriuretic peptide are depressed in obesity despite higher left ventricular end diastolic pressures. *Am Heart J* ;152:1071–6.

24. Iwanaga Y, Kihara Y, Niizuma S, Noguchi T, Nonogi H, Kita T and Goto Y. (2007). BNP in obese and overweight patients with heart failure: an analysis based on the BNP-LV diastolic stress wall relationship. *J Cardiac Fail*;13:663–667.

25. Horwich TB, Hamilton MA and Fonarow GC.(2006). B-type natriuretic peptide levels in obese patients with advanced heart failure. *J Am Coll Cardiol* ;47:85–90.